- 14. (Thrice Amended) A method for sorting nucleic acid, wherein said method comprises:
- (i) digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population, wherein said endonuclease is selected such that each nucleic acid in the resulting nucleic acid population has a sticky end of a known base sequence and of a known common length extending from a terminal of its double-stranded portion, and wherein each nucleic acid in the nucleic acid population has a double-stranded portion;
- (ii) contacting the nucleic acid population with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein said adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population;
- (iii) categorizing the nucleic acid by isolating nucleic acids wherein both termini of the double-stranded portion of said nucleic acid correctly hybridize to an oligonucleotide sequence by contacting a first set of oligonucleotide sequences with the nucleic acid population by:
- (a) denaturing the nucleic acid population in the presence of the first set of oligonucleotide sequences covalently linked to a solid phase support to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first set of oligonucleotide sequences, wherein each oligonucleotide sequence in said first set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide

sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

- (b) immobilizing those nucleic acids which correctly hybridise to the oligonucleotide sequence added to that well;
- (c) extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid;
- (d) denaturing the double-stranded nucleic acid and removing nonimmobilised species to isolate the resulting immobilised single-stranded nucleic acid;
- (e) contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences, wherein each oligonucleotide sequence in said second set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;
- (f) extending the correctly hybridised oligonucleotide sequences along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid;
 - (g) denaturing the double-stranded nucleic acid; and

and

(h) isolating the resulting non-immobilised single-stranded nucleic acid;

Application No. <u>09/462,635</u>

Attorney's Docket No. 020600-285

Page 4

(iv) further sorting the isolated single stranded nucleic acid of step (h) by repeating step (iii) on the isolated single stranded nucleic acid of step (h), wherein the first set of oligonucleotide sequences is replaced by a third set of oligonucleotide sequences, each oligonucleotide sequence of the third set recognizing a further portion of the nucleic acid which was double stranded after digestion with the endonuclease, and wherein the second set of oligonucleotide sequences is replaced by a fourth set of oligonucleotide sequences, each oligonucleotide sequence of the fourth set recognizing a further portion of the nucleic acid which was double stranded after digestion with the endonuclease.